CDC Update: Antimicrobial Resistance

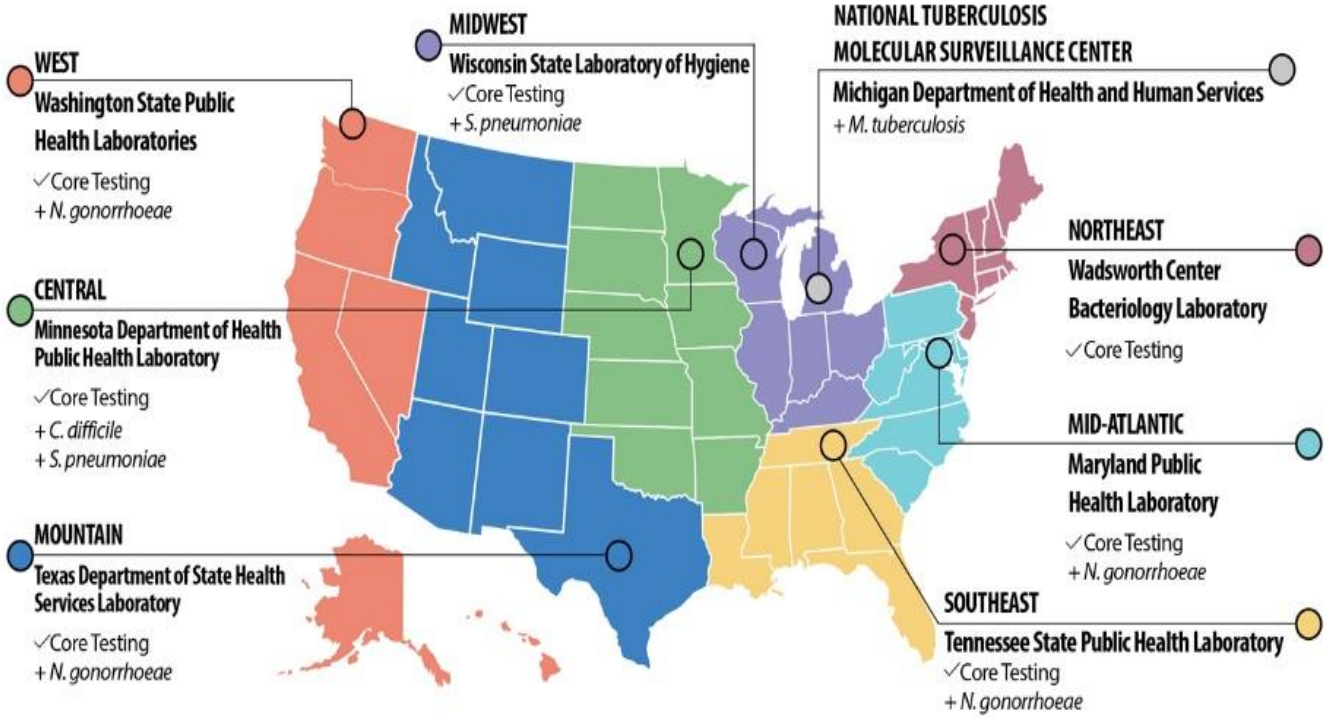
Jean B. Patel, PhD, D(ABMM)
Science Lead, Antibiotic Resistance Strategy and Coordination Unit
Centers for Disease Control and Prevention

AR Lab Network

New Drug Susceptibility Testing

AR Lab Network

Early detection of resistance & testing to support containment



Treating Metallo-β-Lactamase + Enterobacteriaceae Infections

	Drugs for MDRO Gram-Negative Infections	Most Common CRE Types	
		KPC	NDM
FDA-Approved	Colistin	?	?
FDA-Approved	Ceftazidime-Avibactam	✓	X
FDA-Approved	Meropenem-Vaborbactam	✓	X
Phase 2 or 3	Impenem-Relebactam	✓	X
Phase 2 or 3	Plazomycin	✓	?
Phase 2 or 3	Aztreonam-Avibactam	✓	✓
Phase 2 or 3	Cefiderocol	✓	✓

- New data suggests **colistin** may provide little clinical benefit
- NDM-CRE usually carry a gene that confers resistance to all aminoglycosides including **plazomycin**
- **Aztreonam-avibactam** can be created by treating a patient with ceftazidime-avibactam and aztreonam

MBL+ Enterobacteriaceae in the U.S.

- From isolates collected in the AR Lab Network – about 7% of CRE are NDM-positive
- Most common type of CRE world wide
- Treatment options very limited
  - 2018 Stanford Guide recommends ceftazidime-avibactam + aztreonam for treatment of serious infections
- There is no way for hospital labs to test for susceptibility to this drug combination

A Pilot Program – Susceptibility Testing of New Drugs

- **Closes the gap** between new drug approval and the availability of testing methods in hospital laboratories
- **Answers the question, "Will our drugs work?"** HP inkjet printer allows for on-demand reference susceptibility testing of new drugs in regional labs of the AR Lab Network
- **Rapid reporting to improve care** via AR Lab Network IT reporting to hospitals for tailored patient treatment

First application: AST for ceftazidime-avibactam + aztreonam

Launch of New Drug Susceptibility Testing in Regional Laboratories

- First Quarter of 2019
- Information about accessing testing will be
  - Available on the website
  - Shared with healthcare professionals via listserv and professional societies

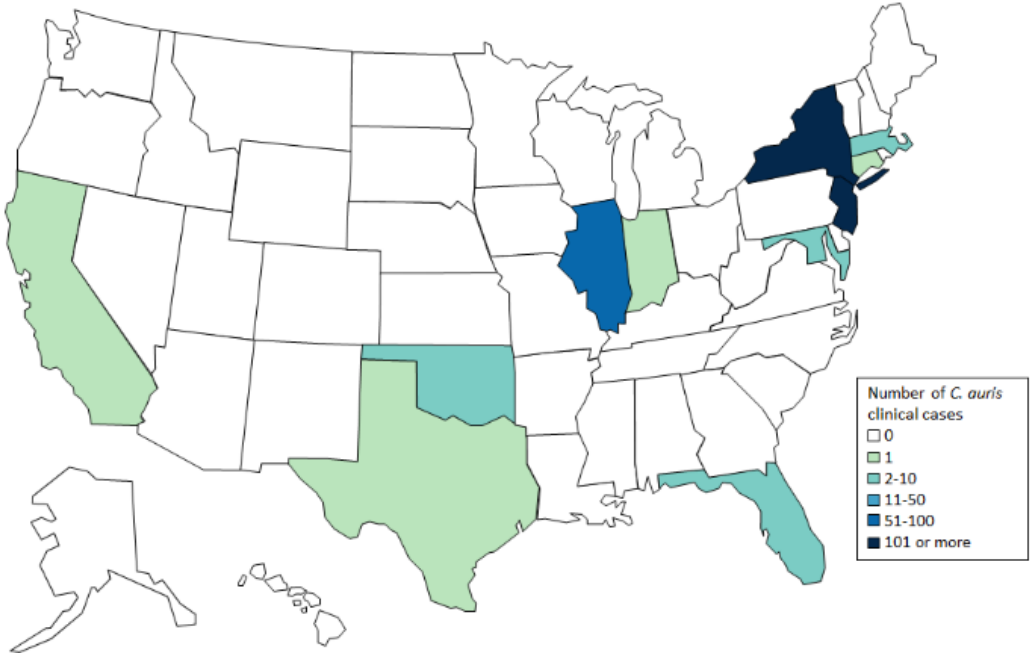
AR Lab Network

PCR for Candida auris Colonization Testing

Candida auris

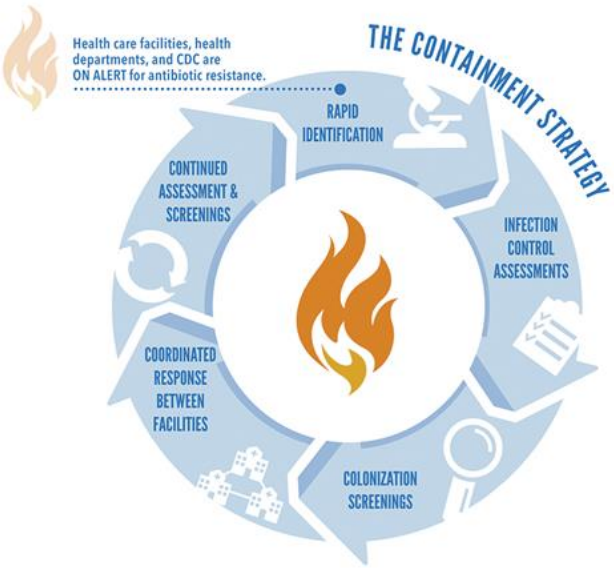
- A fungal pathogen causing healthcare facility outbreaks around the world
- Only recently emerged in the United States with nearly all cases occurring after mid 2016.
- *C. auris* is resistant to multiple antifungal drug classes. Pan-resistant isolates have been identified.
- Outbreaks are challenging to control because both the patients and the hospital environment are readily colonized by *C. auris*

Candida auris Clinical Cases Reported by State United States, September 30, 2018



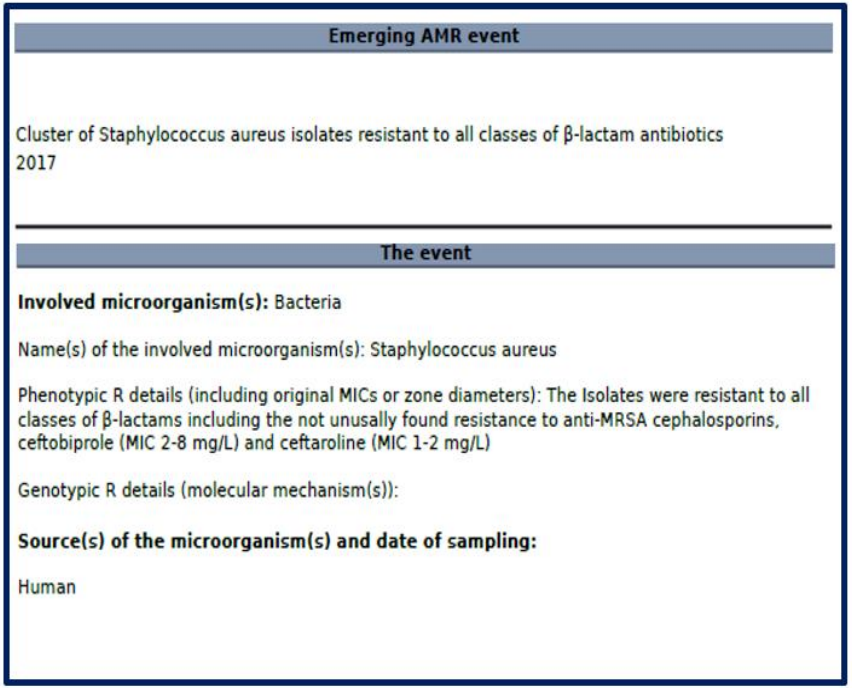
Containment Strategies – *C. auris*

- Colonization Screenings
  - Rapidly implemented in AR Lab Network for *C. auris*
  - CLIA-compliant culture-base method
  - **New:** CLIA-compliant PCR-based method



WHO Global AR Surveillance System Emerging Antimicrobial Resistance – GLASS-EAR

GLASS Emerging AMR Event Simulation



Emerging AMR event

Cluster of Staphylococcus aureus isolates resistant to all classes of β-lactam antibiotics
2017

The event

Involved microorganism(s): Bacteria

Name(s) of the involved microorganism(s): Staphylococcus aureus

Phenotypic R details (including original MICs or zone diameters): The Isolates were resistant to all classes of β-lactams including the not unusally found resistance to anti-MRSA cephalosporins, ceftobiprole (MIC 2-8 mg/L) and ceftaroline (MIC 1-2 mg/L)

Genotypic R details (molecular mechanism(s)):

Source(s) of the microorganism(s) and date of sampling:

Human

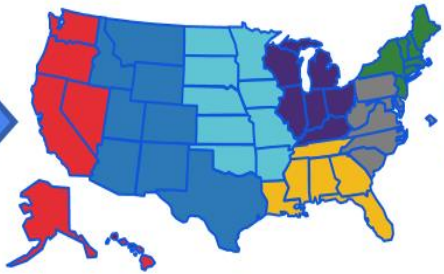
- Communication of new and emerging AR threats across the globe
- Enables local response efforts
- Allows national surveillance program to adjust strategies

Detecting New Types of Resistance – Guidance to Labs

- CLSI M100 Appendix A
  - Three categories
    - Category 1 – Never been seen before
    - Category 2 - Rare
    - Category 3 – Geographical or population differences
  - Phenotypic only
- CLSI is updating Appendix A and the AR Lab Network Alerts Document

Improved Communication of New AR

Sends isolates with unusual resistance to ARLN



Confirms & characterizes resistance. Initiates local prevention efforts

CDC issues a national alert & sends alert to WHO

WHO sends a global alert

A Few Breakpoint Issues

Aligning Disk Content

- CLSI and EUCAST have recommended different disk mass in the past

- Different approaches
  - CLSI relies on the sponsor to pick a disk mass based upon M23 guidance. This is done early in development. The sponsor generates data for disk diffusion breakpoints
  - EUCAST reference lab picks a disk mass late in develop and generates data for disk diffusion breakpoints

- Two different disks for the same drug creates challenges

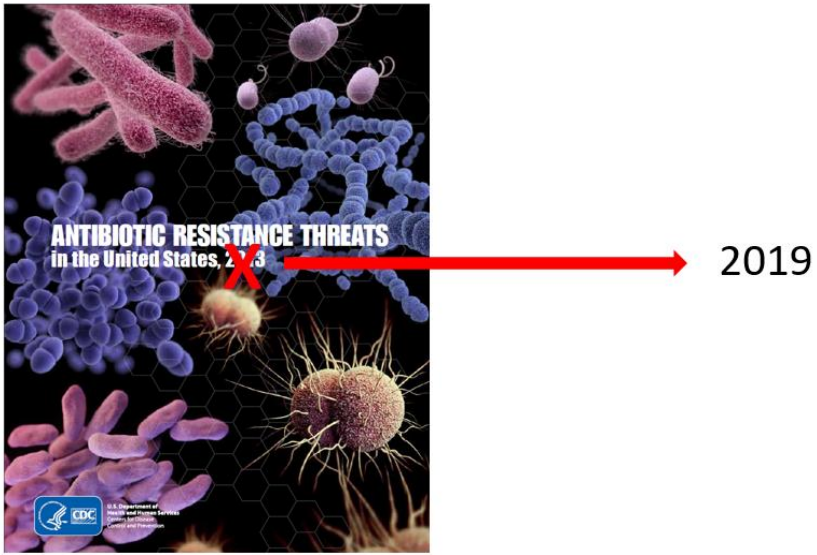
- CLSI-EUCST collaboration to identify a common process and have a single disk per drug moving forward

Still Working on Alignment: Interpretation Categories

CLSI			EUCAST		
Cat	**Meaning**	**Use**	**Cat**	**Meaning**	**Use**
S	Drug should work	All breakpoints	S	Drug should work	All breakpoints
I	Technical variability & high exposure	Often	ATU (new)	Technical variability	Rarely
SDD	S if high exposure (high dose)	Rarely	I	S if high exposure	Often
R	Drug will not work	Most Breakpoints	R	Drug will not work	Most Breakpoints

The Biggest Threats – Follow Up

- The next report in 2019
- New data sources used to report infection rates and mortality estimates
- A new threat category – Urgent, Serious, Concerning, Watching
- AMR in the Environment



Thank You

Jean Patel

jpatel1@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.